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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,768	11/27/2000	Yasuhiko Koezuka	081356/0153	6284

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	7

DATE MAILED: 12/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/721,768	Koezuka
Examiner	**Art Unit**
Leigh Maier	1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 16, 2002 .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-13, 20, and 21 is/are pending in the application.

4a) Of the above, claim(s) 20 and 21 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-13 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2, 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election without traverse of Group I, claims 1-13 in Paper No. 6 is acknowledged. Claims 20 and 21 have been withdrawn from consideration.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by MORITA et al (reference A12).

MORITA discloses culturing mononuclear cells, comprising antigen presenting cells (APCs), from human peripheral blood and umbilical cord blood in the presence of α–galactosylceramides embraced by Formula (A), including KRN7000 (AGL-582 - This is the compound recited in claim 8). See page 2186, last three paragraphs; Scheme 2; page 2179, last full paragraph; and Tables 5 and 6. The α–galactosylceramide concentrations used are 1 ng/mL,

10 ng/mL, and 100 ng/mL. The steps of the method are performed, and thus, the method is accomplished.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over MORITA (reference A12) as applied to claims 1-10 above, in view of KOEZUKA et al (reference A16) and HSU et al (reference A6).

The invention is drawn to the activation of human APCs comprising culturing them *in vitro* in the presence of an α–galactosylceramide. Dependents are drawn to particular species of α–galactosylceramide and concentrations. The method has further limitations requiring the inclusion of cytokines, GM-CSF and IL-4, and a tumor antigen.

MORITA teaches as set forth above. The reference does not explicitly state that the disclosed culturing method results in activated APCs. However, the reference teaches that the cultured cells were used as stimulator cells in an MLR assay and exhibited lymphocyte proliferation (LP) stimulatory effects relative to a control. One of ordinary skill would recognize this as evidence of activated APCs.

KOEZUKA teaches that KRN7000 enhances the APC activity of murine dendritic cells (DCs). The reference also teaches the KRN7000 also stimulates LP of human umbilical cord blood, as discussed above. See entire abstract. This reference suggests equivalent activity of KRN7000 in mice and humans with regard to effectiveness in activating APCs.

HSU teaches the isolation of DCs from blood and treating them with a tumor antigen for the therapeutic use of stimulating antitumor activity. See abstract and page 57, first paragraph. The reference further suggests the addition of cytokines, such as GM-CSF and IL-4, for expanding DCs in culture and increasing immunogenicity. See page 52, third paragraph and page 56, first full paragraph.

It would have been obvious to one having ordinary skill at the time the invention was made to activate APCs, particularly DCs, by culturing them with α–galactosylceramides taught

by MORITA. KOEZUKA teaches that a α–galactosylceramide species (KRN7000) is useful in activating murine DCs and suggests similar results with human DCs. One of ordinary skill would reasonably expect success in preparing activated human APCs by such treatment. The artisan would be motivated to prepare activated DCs, followed by further treatment with the recited cytokines and a tumor antigen to prepare a tumor-specific vaccine as taught by HSU. The combined teachings would give one of ordinary skill a reasonable expectation of success in doing so.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over MORITA (reference A12), in view of KOEZUKA et al (reference A16) and HSU et al (reference A6), as applied to claims 1-11 and 13 above, and further in view of O'DOHERTY et al (J. Exp. Med., 1993).

The invention is as set forth above. Claim 12 recites the limitation requiring culturing in the presence of monocyte conditioned medium (MCM).

MORITA, KOEZUKA, and HSU teach as set forth above. The combination of references do not teach the use of MCM.

O'DOHERTY teaches that culturing DCs in MCM enhances their maturation and immunostimulatory function and increases their viability. See abstract; paragraph bridging pages 1067 and 1068; and 1072, right column.

It would have been obvious to one having ordinary skill at the time the invention was made to activate APCs, particularly DCs, by culturing them with α–galactosylceramides, taught by MORITA, and the other cytokines and a tumor antigen, as set forth above, for use as a tumor vaccine. It would be further obvious to culture the cells in MCM to further aid in cell maturation and activation of immunostimulatory function and increase their viability.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Tuesday, Wednesday, or Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
December 20, 2002